

REMARKS

Claims 13, 15, 17, 18, 25, 26, 29, 30, 33-33, 35, 43, 49-52, 55-60, 62, 63, and 66-73 appear in this application for the Examiner's review and consideration. Claims 13, 29 and 59 have been amended to recite specific embodiments and are supported by the specification and claims as originally filed. Claims 34, 47, 48, 53, 54, 61, 64 and 65 have been canceled. Claims 50, 55-58, and 66-69 have been amended to be consistent with the changes made to claims 13, 29 or 59, as appropriate. Claim 29 has also been amended to correct an informality. Claim 30 has been amended to correct a typographical error. Claims 25, 26, 35, and 62 have been amended to include the structures of the compounds recited therein, support for which is found in Appendix A of the application as filed. Claim 13 is supported, for example, by compounds 7, 20, S7, S20, S27 and S36, Figure 12, and page 8, lines 1-6. Claim 29 and its dependent claims are supported, for example, by compound S36, page 9, line 16 to page 10, line 4, page 11, lines 11-16, page 66, line 3, paragraph [0154], page 71, lines 11-16 and line 18 to page 72, line 3; and Figure 13. Claim 59 and its dependent claims are supported, for example, by compound S36, page 9, line 16 to page 10, line 4, page 11, lines 11-16, page 66, line 3, paragraph [0154], page 71, lines 11-16 and line 18 to page 72, line 3; and Figure 13. New claims 70 and 72 and their dependent claims are supported by, for example, by compounds 7, 20, S7, S20 and S27, page 9, line 16 to page 10, line 4, page 11, lines 11-16, page 66, lines 1-3, paragraph [0154], page 71, lines 11-16 and line 18 to page 72, line 3; and Figure 13. Applicants respectfully submit that no new matter has been introduced by any of these amendments, so that they should be entered at this time.

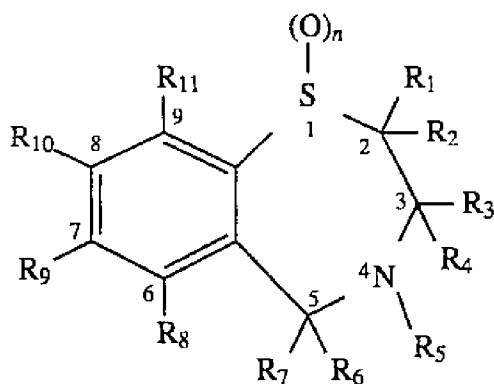
Claim 29 has been objected to because of informalities. In response, the second abbreviation "VT" has been spelled out as "ventricular tachycardia," and the first "VT" deleted. Therefore, the objection has been overcome and should be withdrawn.

Claims 13, 15, 17, 18, 29, 30, 33, 43, 47-60, 63, 64, 65, 67 and 69 have been rejected under 35 U.S.C. 112, first paragraph, allegedly for lack of enabling disclosure. The Examiner acknowledges that the examples disclosed in the specification embody a "common core (that) includes a methoxy at position 3 of the phenyl ring as well as $R_2=H$ and $R_3=H$." Claim 13 has been amended to recite, " $R_1 = OR'$ at position 7 on the benzothiazepine ring; $R' = \text{alkyl}$; $R_2 = H$; $R_3 = H$; $R_4 = \text{halide, alkenyl, carboxylic acid, or an alkyl containing halogen, O or S; and } m = 0, 1, \text{ or } 2$." Claims 29 and 59 have been amended similarly but recite that R_4 is halide, carboxylic

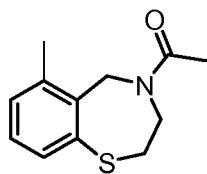
acid, or an alkyl containing O or S. As noted above, these amendments are made solely to expedite the allowance of the present application, without acquiescing in the correctness of the rejection. Claims 13, 29 and 59 as amended and new claims 70 and 72 recite a compound of formula (g) wherein the R_1 is OR' at position 3 of the phenyl ring and wherein R' is alkyl, which is fully enabled by the recitation of R_1 =methoxy in the exemplary compounds S7, S20, S27 and S36. In this rejection, the Examiner alleges that there is no *in vitro* or *in vivo* data for where $m=1$. Applicants respectfully disagree. At the very least, Figure 12 and Example 13 provide *in vitro* data showing that a compound of formula (g) wherein $m=1$, i.e., compound S20, is cable of increasing the binding of FKBP12.6 to RyR2. Thus, the entire rejection has been overcome and should be withdrawn.

Claims 25, 26, 34, 35, 61 and 62 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. In response, claims 25, 26, 34, 35, 61 and 62 have been amended to include the structures of the compounds recited therein as suggested by the Examiner. Therefore, this rejection also has been overcome and should be withdrawn.

Claims 13, 15, 17, 18, 29, 30, 33, 43, 47, 48, 50, 53, 54, 56, 63, 64, 65, 67 and 69 have been rejected under 35 U.S.C. 103(a) as being unpatentable over US patent no. 5,580,866 to Housley et al. (referred to hereafter as "Housley"), in view of Pfammatter et al. Housley discloses a generic structure, as shown below, that covers over 1.2 million compounds.

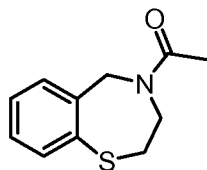


As acknowledged by the Examiner, Housley does not teach the claimed embodiments of the present invention. Moreover, even the specific compounds disclosed in Housley identified by the Examiner as the closest, 4-acetyl-6-methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine

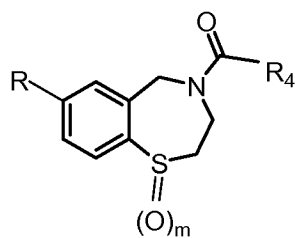


and

4-acetyl-2,3,4,5-tetrahydro-1,4-benzothiazepine



are completely different from the compounds used in the presently claimed methods. For example, the present claims as amended now recite a compound of the formula



, wherein R₁ is OR' and R' is alkyl.

More importantly, Housley does not teach or suggest the use of such compounds for increasing binding of FKBP12.6 to RyR2, reducing the risk of sudden cardiac death and sustained or non-sustained ventricular tachycardia, or for treating cardiac arrhythmias, as presently claimed. Even if the compounds disclosed by Housely were the same as those currently claims (which they are not), there is no disclosure in Housely to use such compounds in the presently claimed methods.

The Office Action states that it would have been obvious to select the “suggested methoxy group” to arrive at “compositions ‘yielding no more than one would expect from such an arrangement’” at page 7. However, the Office Action fails to identify *any* reason that a person skilled in the art would combine elements to arrive at the claimed compounds, much less a reason to believe that a claimed compound would be useful in the claimed methods. For example, the Office Action fails to show why a person skilled in the art would chose an alkoxy group at position 7 of the benzothiazepine ring of the Housely compounds or believe that such compounds would be useful in the claimed methods of the present application. As the Federal Circuit held in *Takeda v. Alphapharm*, “[I]n cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known

compound in a particular manner to establish prima facie obviousness of a new claimed compound.” (84 U.S.P.Q.2d 1197 (Fed. Cir. 2007), citing *KSR v. Teleflex*). The claimed methods of using the claimed compounds are new. Thus, the mere selection of specific substituents from a laundry list with no reason to select those particular substituents or expect that they would lead to the claimed activity is insufficient for the *prima facie* obviousness of the instant claims.

In an attempt to remedy the deficiencies of Housley, the Examiner cited a journal article by Pfammatter et al. (*Cardiac arrhythmias mimicking primary neurological disorders: a difficult diagnostic situation*, Acta Paediatrica, Volume 84, Issue 5, 1995, Pages:569-572, referred to hereinafter as “Pfammatter”). However, neither Housley nor Pfammatter, alone or in combination, teach or suggest the selection of the compounds recited in the claimed methods, nor the methods themselves. Thus, these references do not render the present invention as claimed obvious and the rejection over Housley and Pfammatter should be withdrawn.

Applicants do not acquiesce in the correctness of the rejections or objections, and reserve the right to present specific arguments regarding any rejected or objected-to claims not specifically addressed. Further, Applicants reserve the right to pursue the full scope of the subject matter of previously pending claims in a subsequent patent application that claims priority to the instant application.

CONCLUSION

For at least the reasons set forth above, Applicants respectfully submit that this application is in condition for allowance. Favorable consideration and prompt allowance of the claims are earnestly requested. Should the Examiner have any questions that would facilitate further prosecution or allowance of this application, the Examiner is invited to contact the Applicants' representative designated below. Please charge any necessary fees to deposit account 08-0219.

Respectfully submitted,

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/Jane M. Love, Ph.D./
Jane M. Love, Ph.D.
Reg. No. 42,812

Wilmer Cutler Pickering Hale and Dorr, LLP
399 Park Avenue
New York, New York 10022
Tel: (212) 937-7233
Fax: (212) 230-8888
jane.love@wilmerhale.com